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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,725	09/04/2004	Daniel W Chan	57203(71699)	7047

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EXAMINER	
YAO, LEI	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,725	CHAN ET AL.	
	Examiner	Art Unit	
	LEI YAO	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/4/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-5,7-13,16-19,21,24-29,31,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7-13, 16-19, 21, 24-29, 31, 58, and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Response to Amendment and Arguments

The Amendment filed on 12/4/2008 in response to the previous Non-Final Office Action (6/4/2008/2008) is acknowledged and has been entered.

Claim 59 is added.

Claims 6, 14, 15, 20, 22, 23, 30, 32-57 are cancelled.

Claims 1-5, 7-13, 16-19, 21, 24-29, 31, 58, and 59 are pending and method of qualifying or determining a breast cancer by measuring at least one marker (elect BC3) and a method of measuring of a plurality of biomarkers comprising BC3 (elected), are under consideration.

Rejections Withdrawn

The rejection of claims 1, 2, 4, 5, 7, 13, 16, 17, 23, 25, and 58 under 35 U.S.C. 102(b) as being anticipated by Watson et al., is withdrawn in view of the amendments to the claims.

Rejections/Objection Maintained and Response to Arguments

Claim Objection

Claims 1-5, 7-13, 16-19, 21, 24-29, 31, 58, and 59 remain objected to as stated in the previous Office because amended claims still contain abbreviations for biomarkers, BC1, BC2, and BC3, which are neither recognized names or structures in the art or nor defined in the specification.

Applicant requests the objection be withdrawn in view of the amendment. The request is considered, however, currently amended claims of adding molecular weight does not provide full names of these abbreviations as well as the structural information for those biomarkers. Applicant is noted if BC stands for a breast cancer biomarker, spell out first time used in the claims are appreciated.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement Rejection:

Claims 1-5, 7-13, 16-19, 21, 24-25, and 58 remain and claim 59 is currently rejected under 35 U.S.C. 112, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Response to Applicant's argument:

Applicant (page 9) lists teachings of the specification on the biomarkers, BC1-3 identified by SELDI-mass spectroscopy, in the samples of breast cancer patients. Applicant on page 10-11 further argues the examples in the specification in order to

support the claimed method. These have been carefully considered but are deemed not to be persuasive to overcome the rejection for the following reasons:

1) The biomarkers having MW about 4283, (BC-1), about 8126 (BC-2) and about 8932 (BC-3) are not used as recognized marker for any cancer including breast cancer. The specification does not disclose the structure and sequence of those markers. One could find many proteins presented in the serum samples of breast cancer patients which could be broken to fragments having such molecule weight when they are applied to mass spectroscopy.

2) The tables in the specification summarize the intensity of the peak of each marker that does not fully support the claimed method (page 10 of remarks, specification, page 58, examples 4-5). For example, line 1 of BC1 marker, the standard deviation for the intensity of the BC1 marker is larger than the intensity of the marker self. Line 2 of BC-2 also shows no significant difference between the non-cancer control and breast cancer patients if the standard deviation are taken into a consideration. As such, one could not determine what the cut off value of the intensity is to determine or diagnose whether a patient has or not a breast cancer.

3) More important, the Office provides teaching of the arts indicating that the markers are not validated as breast cancer markers for diagnosing and some of the arts are inventor's own publication. Specifically, the arts teaches BC1-3 are truncated form of complement C3a that is very short lived in serum and is cleaved immediately into the more stable form. BC-1 could not be used as biomarker for breast cancer detection because the reference of Li et al (2002) teaches that BC1 decreases in breast cancer,

whereas another reference of Li et al published in 2005, teaches that an increase of BC1 was associated with the breast cancer as stated in the rejection.

Regarding to these publications, Applicant first argues: each of these references was published after the priority date of the instant specification. In response, using later published art as evidence to support an enablement rejection is proper as stated in the section of MPEP 2164.05:

> **If individuals of skill in the art state that a particular invention is not possible years after the filing date, that would be evidence that the disclosed invention was not possible at the time of filing and should be considered.**

Applicant then argues the reference of Li et al (Clin Chem 2005), who state on page 2234, second column, "BC1 may still be a valid marker if sera were collected prospectively ands stored under the same conditions". In response, both this reference and reference of Li (2002) indicate that BC-1 has inconsistent expression in breast cancer samples and suggest that variation is most likely the causes of the discrepancies (see rejection). If Applicant believes that the storage is a concern for the inconsistency of the results, the issue of sample collection and storage should be stated in the current specification. Actually, Applicant here gives another reason that the BC-1 as a biomarker for breast cancer is unpredictable because of no guideline and direction how the samples are collected or stored.

Regarding the marker of BC-2 and BC-3, Applicant states "the examples of the specification provide that BC-2 and BC-3 can discriminate between benign and cancer tissues, which has been discussed above. In addition, in the rejection the Office has

provided the teachings of arts on that the marker could not be used for breast cancer detection because high or low concentrations of the proteins were reported in wide variety of clinical conditions. The art also questions the clinical value whether those markers are non-specific markers (page 5 of Office action). Applicant does not comment on these references.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 4-8, 10, 11, 17-19, 21, 23, 24, 26-28, 30 and 58 remain and claim 59 is rejected under 35 U.S.C. 102(e) as being anticipated by Mutter et al., (US Patent No. 6703204, priority to July 28, 2000).

Newly added claim 59 is further drawn to claim 58, further comprising a managing subject treatment based on the presence or absence of breast cancer.

Mutter et al also provide a method of treatment for breast cancer after diagnosis (example, col 19+).

Applicant argues that the claims have been amended to indicate the biomarkers of the instant invention being identified by mass spectrometry and molecular weight of each marker. In response, the amendment is considered, but could not overcome the rejection because Mutter et al disclose a plurality of biomarkers including a biomarker has MW about 8000 daltons measured by SELDI mass spectrum, which meets the limitation in the amendment reciting molecular weight about 8126, or even 8932. The term "about 8126" and "about 8932" does not define up and low limitation of the molecular weights. Therefore, the Mutter et al still anticipate claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 8-12, 26, and 29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mutter et al., (US Patent No. 6703204, priority to July 28, 2000) in view of Lauro et al (Anticancer Res. vol 19, page 3511-5, 1999, abstract) and/or Gion et al., (Clin. Chem. vol 45, page 630-637, 1999).

Applicant provides the same argue as the 102 rejection by Mutter et al, which would be responded the same as above.

Thus, Applicant's argument has not been found persuasive, and the rejections are maintained currently.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lei Yao, Ph.D. whose telephone number is 571-272-3112. The examiner can normally be reached on 8am-6.00pm Monday-Thursday.

Any inquiry of a general nature, matching or file papers or relating to the status of this application or proceeding should be directed to Kim Downing for Art Unit 1642 whose telephone number is 571-272-0521

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Lei Yao/
Examiner, Art Unit 1642

/Larry R. Helms/
Supervisory Patent Examiner, Art Unit 1643